

REMARKS

Claims 1, 4, 9, 11-16, 20, 22-28, 34-36, 40 and 41 were pending prior to this Response. The Office Action incorrectly lists claims 10 and 21 as pending. Claims 10 and 21 were cancelled in the Response filed by Applicants on October 6, 2003. By the present communication, page 75 of Table 4 of the Specification has been amended to correct an obvious error in SEQ ID NO:69. In addition, no claims have been added or cancelled and claim 28 has been amended to define Applicants' invention with greater particularity. The amendments add no new matter, being fully supported by the Specification and original claims. Accordingly, claims 1, 4, 9, 11-16, 20, 22-28, 34-36, 40 and 41 are currently pending in this application.

The Declaration

The Examiner asserts that the declaration filed January 31, 2003 is defective because it incorrectly claims priority to a non provisional application under 35 U.S.C. § 119(e) rather than 35 U.S.C. § 120. To overcome the rejection, Applicants submit herewith an executed Declaration that correctly claims priority to the application Serial No. 09/771,357 under 35 U.S.C. § 120. Accordingly, Applicants respectfully request withdrawal of the objection to the declaration.

The Objection to the Specification

The Office Action contains an objection to the Specification for alleged failure of the sequence of SEQ ID NO:69 as presented in Figure 5C to match the sequence in the sequence listing or the table on page 75 of the Specification. By the present communication, Applicants have amended the sequence of SEQ ID NO:69 in Table 4 at page 75 to add a missing nucleotide (G) between residues 7 and 8. Applicants submit that, with this amendment, the sequence of SEQ ID NO:69 is corrected at page 75 of the Specification and is now matches that in Figure 5C, and in the sequence listing.

In view of the amendment, Applicants respectfully request reconsideration and withdrawal of the objection to the Specification.

The Rejection under 35 U.S.C. § 112, First Paragraph

Applicants respectfully traverse the rejection of claims 28, 34-36 and 40-41 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. Applicants disagree with the Examiner's assertion that the Specification fails to provide sufficient description to enable those of skill in the art to make or use the invention commensurate in scope with the previously presented claims. For example, Applicants disagree that in claim 28 comparison of hypermethylation of at least one CpG island in the promoter of RARB2 in a subject is compared to *any* sample from a normal subject because previously presented claim 28 required that comparison of the subject's DNA with the methylation state of "the same region of the same nucleic acid" in the control sample.

However, to expedite prosecution and reduce the issues, Applicants have amended previously presented claim 28 to adopt the language the Examiner acknowledges (Office Action, page 3, top) is enabled by the Specification, by reciting: "wherein the CpG islands in the promoter of RAR β 2 is hypermethylated compared to the methylation state of CpG islands in comparable samples obtained from normal subjects." Thus, the "control" is not limited to breast tissue of a single normal individual, but is required to be representative of nucleic acids obtained from a plurality of normal, i.e., the absence of hypermethylation in CpG islands in the promoter of RAR β 2 nucleic acids in a broad population of normal subjects. In view of the amendment to claim 28, Applicants submit that the rejection is rendered moot as to the subject matter of claims 28, 34-36 and 40-41 and reconsideration and withdrawal of the rejection for alleged lack of enablement is respectfully requested.

The Rejection under 35 U.S.C. § 102(a)

A. Applicants respectfully traverse the rejection of claims 1, 4, 9-16, 20-28, 34-36 and 40-41 under 35 U.S.C. § 102(a) as allegedly being anticipated by Sirchia et al. (*Oncogene*, 19:1556-1563, March 16, 2000; hereinafter "Sirchia"). Claims 10 and 21 have previously been cancelled without prejudice, rendering the rejection moot as to the subject matter of these claims. The rejection will now be discussed with regard to pending claims 1, 4, 9, 11-16, 20, 22-28, 34-36, and 40-41.

Applicants have previously submitted a Declaration under 35 U.S.C. § 131 signed by Saraswati Sukumar stating that the co-inventors of the present application, and of the prior application on which it relies, conceived and reduced the invention methods to practice in the United States prior to the date of publication of the Sirchia article. Moreover, the Declaration states that Nicoletta Sacchi, who is named as one of the co-authors of the Sirchia et al. reference, is one of the co-inventors of the present application and contributed to conception of the invention described in the priority application. By contrast, Silvia M. Sirchia, Anne T. Ferguson, Elena Sironi, Smitha Subramanyan and Rosaria Orlandi, who are named as co-authors of the Sirchia article, contributed to the research effort that led to the Sirchia reference, but did not contribute to conception of the invention as described in the present application or as described in the priority application.

However, the Examiner has requested that the Declaration be executed by all of the co-inventors of this application. Accordingly, submitted herewith is a revised Declaration under 35 U.S.C. § 1.131 signed by all of the co-inventors herein. In view of the revised Declaration under 35 U.S.C. 1.131 and the above remarks, Applicants respectfully submit that the disclosure of Sirchia that is relied upon in the rejection of claims of the present application for alleged anticipation was conceived and reduced to practice by the co-inventors of the present application prior to the date of publication of the Sirchia reference. Accordingly, Sirchia is not available as

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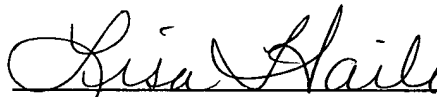
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prior art under 35 U.S.C. 102(a) and reconsideration and withdrawal of the rejection are respectfully requested.

In view of the above amendments and remarks, Applicants submit that all rejections of the claims are overcome and Applicants request favorable action on all pending claims. If the Examiner would like to discuss any of the issues raised in the Office Action, the Examiner is encouraged to call the undersigned so that a prompt disposition of this application can be achieved.

Respectfully submitted,

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Enclosures: Executed Declaration of Inventors
Revised and executed Declaration under 35 U.S.C. § 1.131